

Amendments to the Claims under Revised 37 C.F.R. § 1.121

Claim 1 (currently amended): A truncated sTNFR polypeptide comprising:

(a) _____ amino acid residues 1-110, 1-109, 1-108, 1-107, 1-106, 1-105, 1-104, 1-103, 2-110, 2-109, 2-108, 2-107, 2-106, 2-105, 2-104, 2-103, 3-110, 3-109, 3-108, 3-107, 3-106, 3-105, 3-104, 3-103, 4-110, 4-109, 4-108, 4-107, 4-106, 4-105, 4-104, 4-103, 5-110, 5-109, 5-108, 5-107, 5-106, 5-105, 5-104, 5-103, 6-110, 6-109, 6-108, 6-107, 6-106, 6-105, 6-104, 6-103, 7-110, 7-109, 7-108, 7-107, 7-106, 7-105, 7-104, 7-103, 8-110, 8-109, 8-108, 8-107, 8-106, 8-105, 8-104, 8-103, 9-110, 9-109, 9-108, 9-107, 9-106, 9-105, 9-104, 9-103, 10-110, 10-109, 10-108, 10-107, 10-106, 10-105, 10-104, 10-103, 11-110, 11-109, 11-108, 11-107, 11-106, 11-105, 11-104, 11-103, 12-110, 12-109, 12-108, 12-107, 12-106, 12-105, 12-104, 12-103, 13-110, 13-109, 13-108, 13-107, 13-106, 13-105, 13-104, 13-103, 14-110, 14-109, 14-108, 14-107, 14-106, 14-105, 14-104, 14-103, 15-110, 15-109, 15-108, 15-107, 15-106, 15-105, 15-104, 15-103, 16-110, 16-109, 16-108, 16-107, 16-106, 16-105, 16-104, 16-103, 17-110, 17-109, 17-108, 17-107, 17-106, 17-105, 17-104, 17-103, 18-110, 18-109, 18-108, 18-107, 18-106, 18-105, 18-104, 18-103, 19-110, 19-109, 19-108, 19-107, 19-106, 19-105, 19-104, or 19-103 of SEQ ID NO: 2;

~~or variants and derivatives thereof;~~ provided however, that when the truncated sTNFR polypeptide comprises amino acid residues 1-110, 2-110, 3-110, 4-110, 5-110, 6-110, 7-110, 8-110, 9-110, 10-110, 11-110, 12-110, 13-110, 14-110, 15-110, 16-110, 17-110, 18-110, or 19-110 of SEQ ID NO: 2, the polypeptide does not further comprise amino acid residues 111-161 of SEQ ID NO: 2, or a portion thereof;

(b) _____ the amino acid sequence of (a) with at least one amino acid substitution;

(c) _____ the amino acid sequence of (a) with at least one amino acid addition; or

(d) _____ the amino acid sequence of (a) with at least one internal intrasequence amino acid deletion;

and optionally further comprising an amino-terminal methionine.

Claim 2 (currently amended): An isolated truncated sTNFR polypeptide ~~tumor necrosis binding protein~~ comprising:

(a) _____ the amino acid sequence as set forth in SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID

NO: 8, SEQ ID NO: 12, SEQ ID NO: 10, or SEQ ID NO: 14; ~~or a variant or derivative thereof~~

(b) the amino acid sequence of (a) with at least one amino acid substitution;

(c) the amino acid sequence of (a) with at least one amino acid addition, provided that the polypeptide does not comprise amino acid residues 111-161 of SEQ ID NO: 2 or a portion thereof; or

(d) the amino acid sequence of (a) with at least one internal intrasequence amino acid deletion.

Claim 3 (cancelled).

Claim 4 (currently amended): The polypeptide ~~tumor necrosis binding protein~~ according to ~~any one of either~~ Claim[[s]] 1 ~~through 3 or 2~~, wherein said amino acid sequence is nonglycosylated.

Claim 5 (currently amended): The polypeptide ~~tumor necrosis binding protein~~ according to ~~any one of either~~ Claim[[s]] 1 ~~through 3 or 2~~, wherein said amino acid sequence is glycosylated.

Claim 6 (currently amended): The polypeptide ~~tumor necrosis binding protein~~ according to ~~any one of either~~ Claim[[s]] 1 ~~through 5 or 2~~, wherein the protein is conjugated to a water soluble polymer.

Claim 7 (currently amended): A polyvalent truncated sTNFR molecule ~~tumor necrosis binding protein~~ comprising at least one polypeptide ~~tumor necrosis binding protein~~ according to ~~any one of either~~ Claim[[s]] 1 ~~through 6 or 2~~.

Claim 8 (currently amended): A polyvalent molecule ~~tumor necrosis binding protein~~ having the formula R_1-X-R_2 , wherein:

X comprises a linker, wherein said linker is a water soluble polymer; and

R_1 and R_2 are biologically-active molecules covalently bonded to said water soluble

polymer, wherein at least one of R₁ and R₂ is a polypeptide ~~tumor necrosis binding protein~~ according to any one of either Claim[[s]] 1 through 6 or 2.

Claim 9 (currently amended): The polyvalent molecule ~~tumor necrosis binding protein~~ of Claim 8, wherein the water soluble polymer is polyethylene glycol.

Claim 10 (currently amended): The polyvalent molecule ~~tumor necrosis binding protein~~ of Claim 9, wherein ~~the protein is selected from the group consisting of sTNFR-I 2.6D/C105db and sTNFR-I 2.6D/C106db~~ R₁ and R₂ are polypeptides comprising:

- (a) the amino acid sequence as set forth in SEQ ID NO: 4; or
- (b) the amino acid sequence as set forth in SEQ ID NO: 6.

Claim 11-21 (cancelled).

Claim 22 (currently amended): A truncated sTNFR polypeptide ~~tumor necrosis binding protein~~ which is the recombinant expression product of a prokaryotic or eukaryotic host cell containing an exogenous polynucleotide ~~of any one of Claims 13 through 15~~ encoding the polypeptide of either Claim 1 or 2.

Claim 23 (currently amended): A pharmaceutical composition comprising the polypeptide ~~tumor necrosis factor binding protein~~ according to any one of either Claim[[s]] 1 through 10 or 2 in association with a pharmaceutically acceptable vehicle.

Claim 24 (currently amended): A pharmaceutical composition comprising:
A) the ~~tumor necrosis factor binding protein~~ a polypeptide produced in accordance with the method of Claim 18 by a process comprising the steps of growing a prokaryotic or eukaryotic host cell containing a polynucleotide encoding the polypeptide of either Claim 1 or 2 in a suitable nutrient medium and, optionally, isolating the polypeptide from the host cell or nutrient medium; and

- B) in association with a pharmaceutically acceptable vehicle.

Claim 25 (currently amended): A pharmaceutical composition comprising:

A) the tumor necrosis factor binding protein a polypeptide produced in accordance with the method of Claim 21 by a process comprising the steps of:

(a) culturing a prokaryotic or eukaryotic host cell containing a polynucleotide encoding the polypeptide of either Claim 1 or 2;

(b) maintaining the host cell under conditions allowing the expression of the polypeptide by the host cell; and

(c) optionally isolating the polypeptide expressed by the host cell; and

B) in association with a pharmaceutically acceptable vehicle.

Claims 26 and 27 (cancelled).

Claim 28 (currently amended): A method of preparing a pharmaceutical composition wherein a therapeutically effective amount of the polypeptide tumor necrosis factor binding protein according to any one of either Claim[[s]] 1 through 10 or 2 is mixed with one or more pharmaceutically acceptable vehicles.

Claims 29 and 30 (cancelled).

Claim 31 (currently amended): A kit for preparing an aqueous protein formulation comprising the polypeptide tumor necrosis factor binding protein according to any one of either Claim[[s]] 1 through 10 or 2 and a second container having a physiologically acceptable solvent.

Claim 32 (new): The polypeptide of either Claim 1 or 2, wherein the protein is fused to a heterologous amino acid sequence.

Claim 33 (new): The polypeptide of Claim 32, wherein the heterologous amino acid sequence is an IgG constant domain or fragment thereof.

Claim 34 (new): A truncated sTNFR polypeptide which is the recombinant expression product of a prokaryotic or eukaryotic host cell containing an exogenous polynucleotide comprising a nucleotide sequence:

- (a) as set forth in SEQ ID NO: 3;
- (b) as set forth in SEQ ID NO: 5;
- (c) as set forth in SEQ ID NO: 7;
- (d) as set forth in SEQ ID NO: 11;
- (e) as set forth in SEQ ID NO: 9;
- (f) as set forth in SEQ ID NO: 13;
- (g) that is degenerate in the coding regions or portions thereof of the nucleotide sequence of any of (a) - (f); or
- (h) that hybridizes to the complement of the nucleotide sequence of any of (a) - (g);
provided however, that the polypeptide does not comprise amino acid residues 111-161 of SEQ ID NO: 2, or a portion thereof;
and optionally further comprising a nucleotide sequence encoding an amino-terminal methionine.

Claim 35 (new): A truncated sTNFR polypeptide which is the recombinant expression product of a prokaryotic or eukaryotic host cell containing an exogenous polynucleotide comprising a nucleotide sequence as set forth in SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 11, SEQ ID NO: 9, or SEQ ID NO: 13, or a portion thereof.

Claim 36 (new): A pharmaceutical composition comprising:

- A) a polypeptide produced by a process comprising growing a prokaryotic or eukaryotic host cell containing a polynucleotide comprising a nucleotide sequence:
 - (a) as set forth in SEQ ID NO: 3;
 - (b) as set forth in SEQ ID NO: 5;
 - (c) as set forth in SEQ ID NO: 7;
 - (d) as set forth in SEQ ID NO: 11;
 - (e) as set forth in SEQ ID NO: 9;

- (f) as set forth in SEQ ID NO: 13;
- (g) that is degenerate in the coding regions or portions thereof of the nucleotide sequence of any of (a) - (f); or
- (h) that hybridizes to the complement of the nucleotide sequence of any of (a) - (g);

provided however, that the polypeptide does not comprise amino acid residues 111-161 of SEQ ID NO: 2, or a portion thereof;

and optionally further comprising a nucleotide sequence encoding an amino-terminal methionine;

in a suitable nutrient medium and, optionally, isolating the polypeptide from the host cell or nutrient medium; and

B) a pharmaceutically acceptable vehicle.

Claim 37 (new): A pharmaceutical composition comprising:

A) a polypeptide produced by a process comprising growing a prokaryotic or eukaryotic host cell containing a polynucleotide comprising a nucleotide sequence as set forth in SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 11, SEQ ID NO: 9, or SEQ ID NO: 13, or a portion thereof, in a suitable nutrient medium and, optionally, isolating the polypeptide from the host cell or nutrient medium; and

B) a pharmaceutically acceptable vehicle.

Claim 38 (new): A pharmaceutical composition comprising:

A) a polypeptide produced by a process comprising:

(a) culturing a prokaryotic or eukaryotic host cell containing a polynucleotide comprising a nucleotide sequence:

- (i) as set forth in SEQ ID NO: 3;
- (ii) as set forth in SEQ ID NO: 5;
- (iii) as set forth in SEQ ID NO: 7;
- (iv) as set forth in SEQ ID NO: 11;
- (v) as set forth in SEQ ID NO: 9;

- (vi) as set forth in SEQ ID NO: 13;
- (vii) that is degenerate in the coding regions or portions thereof of the nucleotide sequence of any of (i) - (vi); or
- (viii) that hybridizes to the complement of the nucleotide sequence of any of (i) - (vii);

provided however, that the polypeptide does not comprise amino acid residues 111-161 of SEQ ID NO: 2, or a portion thereof;

and optionally further comprising a nucleotide sequence encoding an amino-terminal methionine;

- (b) maintaining the host cell under conditions allowing the expression of the polypeptide by the host cell; and
 - (c) optionally isolating the polypeptide expressed by the host cell; and
- B) a pharmaceutically acceptable vehicle.

Claim 39 (new): A pharmaceutical composition comprising:

- A) a polypeptide produced by a process comprising:
 - (a) culturing a prokaryotic or eukaryotic host cell containing a polynucleotide comprising a nucleotide sequence as set forth in SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID NO: 7, SEQ ID NO: 11, SEQ ID NO: 9, or SEQ ID NO: 13, or a portion thereof, in a suitable nutrient medium;
 - (b) maintaining the host cell under conditions allowing the expression of the polypeptide by the host cell; and
 - (c) optionally isolating the polypeptide expressed by the host cell; and
- B) a pharmaceutically acceptable vehicle.

Claim 40 (new): The polypeptide of Claim 6, wherein the water soluble polymer is polyethylene glycol.

Claim 41 (new): A pharmaceutical composition comprising the polyvalent truncated sTNFR molecule of Claim 7 in association with a pharmaceutically acceptable vehicle.

Claim 42 (new): A method of preparing a pharmaceutical composition wherein a therapeutically effective amount of the polyvalent truncated sTNFR molecule of Claim 7 is mixed with one or more pharmaceutically acceptable vehicles.

Claim 43 (new): A kit for preparing an aqueous protein formulation comprising the polyvalent truncated sTNFR molecule of Claim 7 and a second container having a physiologically acceptable solvent.

Claim 44 (new). The polypeptide of either Claim 1 or 2, wherein the amino acid substitution, amino acid addition, or intrasequence amino acid deletions do not occur in the first two disulfide loops of domain 1, the whole of domain 2, or the first disulfide loop of domain 3 of the polypeptide.